various concentrations of drug for 48 hours. The time at which compounds are added is considered T_0. A tetrazolium-based assay using the reagent 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(**4**--sulfophenyl)-2H-tetrazolium ((MTS) (U.S. Pat. No. 5,185,450) (see Promega product catalog #G3580, CellTiter 96® (AQ_{ucous} One Solution Cell Proliferation Assay) was used to determine the number of viable cells at T_0 and the number of cells remaining after 48 hours compound exposure. The number of cells remaining after 48 hours was compared to the number of viable cells at the time of drug addition, allowing for calculation of growth inhibition.

[**0637**] The growth over 48 hours of cells in control wells that had been treated with vehicle only (0.25% DMSO) is considered 100% growth and the growth of cells in wells with compounds is compared to this.

[**0638**] A Gi_{50} was calculated by plotting the concentration of compound in μM vs the percentage of cell growth in treated wells. The Gi_{50} calculated for the compounds is the estimated concentration at which growth is inhibited by 50% compared to control, i.e., the concentration at which:

$$100\times[(Treated_{48}-T_0)/(Control_{48}-T_0)]=50$$

[**0639**] wherein $Treated_{48}$ is the value at 48 hours for the treated cells and $Control_{48}$ is the value at 48 hours for the control population.

[**0640**] All concentrations of compounds are tested in duplicate and controls are averaged over 12 wells. A very similar 96-well plate layout and Gi_{50} calculation scheme is used by the National Cancer Institute (see Monks, et al., J. Natl. Cancer Inst. 83:757-766 (1991)). However, the method by which the National Cancer Institute quantitates cell number does not use MTS, but instead employs alternative methods.

[**0641**] Compounds of Examples 1-13 above inhibited cell proliferation in human ovarian tumor cell lines (SKOV-3).

Example 26

[**0642**] Calculation of IC_{50} :

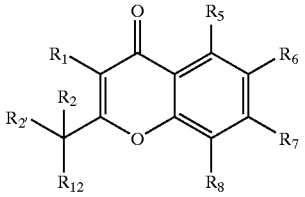
[**0643**] Measurement of a compound's IC_{50} for KSP activity uses an ATPase assay. The following solutions are used: Solution 1 consists of 3 mM phosphoenolpyruvate potassium salt (Sigma P-7127), 2 mM ATP (Sigma A-3377),1 mM IDTT (Sigma D-9779), 5 μM paclitaxel (Sigma T-7402), 10 ppm antifoam 289 (Sigma A-8436), 25 mM Pipes/KOH pH 6.8 (Sigma P6757), 2 mM MgC12 (VWR JT400301), and 1 mM EGTA (Sigma E3889). Solution 2 consists of 1 mM NADH (Sigma N8129), 0.2 mg/ml BSA (Sigma A7906), pyruvate kinase 7 U/ml, L-lactate dehydrogenase 10 U/ml (Sigma P0294), 100 nM KSP motor domain, 50 μg/ml microtubules, 1 mM DTT (Sigma D9779), 5 μM paclitaxel (SigmaT7402), 10 ppm antifoam 289 (Sigma A-8436), 25 mM Pipes/KOH pH 6.8 (Sigma P6757), 2 mM MgC12 (VWR JT4003-01), and 1 mM EGTA (Sigma E3889). Serial dilutions (8-12 two-fold dilutions) of the compound are made in a 96-well microtiter plate (Cornling Costar 3695) using Solution 1. Following serial dilution each well has 50 μl of Solution 1. The reaction is started by adding 50 μl of solution 2 to each well. This may be done with a multichannel pipettor either manually or with automated liquid handling devices. The microtiter plate is then transferred to a microplate absorbance reader and multiple absorbance readings at 340 nm are taken for each well in a kinetic mode. The observed rate of change, which is proportional to the ATPase rate, is then plotted as a function of the compound concentration. For a standard IC_{50} (determination the data acquired is fit by the following four parameter equation using a nonlinear fitting program (e.g. Grafit 4):

$$y = \frac{\text{Range}}{1+\left(\frac{x}{IC_{50}}\right)^{s}} + \text{Background}$$

[**0644**] where y is the observed rate and x is the compound concentration.

What is claimed is:

1. A compound having the structure:



wherein:

R_1 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

R_2 and $R_{2'}$ are independently chosen from hydrogen, optionally substituted alkyl-, optionally substituted alkoxy, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl; or R_2 and $R_{2'}$ taken together form an optionally substituted 3- to 7-membered ring;

R_{12} is selected from the group consisting of optionally substituted imidazolyl, optionally substituted imidazolinyl, —NHR_4; —$N(R_4)(COR_3)$; —$N(R_4)(SO_2R_{3a})$; and —$N(R_4)(CH_2R_{3b})$;

R_3 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, $R_{15}O$— and R_{17}—NH—;

R_{3a} is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, and R_{17}—NH—;

R_{3b} is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl;

R_4 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted hetercyclyl-, and optionally substituted heteroaralkyl-;